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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
05/20/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/581,183	TSUNODA ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-18 and 21-45* is/are pending in the application.

4a) Of the above claim(s) *3,6,21 and 23-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-18 and 22* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/16/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' response of February 16, 2010, to the non-final office Action dated August 14, 2009 has been entered. Claims 1, 5, 8, 14, 15, 22 and 23 have been amended, claims 2, 4, 19 and 20 cancelled, and claims 40-45 newly added. Accordingly, claims 1-3, 5-18 and 21-45 are pending in the application. Claims 3, 6, 21 and 23-39 stand withdrawn from further consideration with traverse, as being drawn to a nonelected invention. New claims 40-45 are additionally withdrawn from consideration as directed to nonelected subject matter, because in the response to the restriction election requirement dated March 2, 2009, Applicants elected without traverse, Group I claims drawn to a DNA construct wherein a mammalian β-actin promoter is operably linked to an enhancer. New base claims 40 and 43 are directed to constructs lacking an operably linked CMV enhancer. Further, claims depending from claims 40 and 43 do not require that the CMV enhancer be operably linked to the mouse β-actin promoter. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. The claims have been examined commensurate with the elected species of the invention.

The instant claims have been examined commensurate with the scope of the elected species of the invention.

Claims 1, 5, 7-18 and 22 are under current examination

Information Disclosure Statement

The information disclosure statement (IDS) submitted on February 16, 2010 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner, and indicated as such on Applicants' IDS form.

Withdrawn Objection to the Specification

The disclosure was objected to in the previous Office action dated August 14, 2009 for containing embedded hyperlinks. Applicants have amended the specification to delete the hyperlinks. Thus, the objection is hereby withdrawn.

Claim Rejections - 35 USC § 112- Second Paragraph

Claims 14-16 were previously rejected under 35 U.S.C. 112, second paragraph, as being indefinite, in the Office action dated August 14, 2009. Applicants have amended claims 14 and 15 to provide for proper antecedent basis, thereby obviating the ground for rejection. Thus, the rejection is hereby withdrawn.

New Claim Objection

Claim 5 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response, Maintained & Withdrawn Claim Rejections - 35 USC § 103

Claims 1, 7, 8, 12, 13, 17, 18 and 22 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Hadjantonakis et al. (Mech. Develop. 76:79-90, 1998), in view of Estes et al. (U.S. Patent No.: 7,423,135; effective filing date Jun. 24, 2003). Applicants' cancellation of claims 2, 4 and 19 renders their rejections moot. The rejection set forth on pp. 4-5 of the previous Office action dated August 14, 2009 is maintained for reasons of record.

The Declaration under 37 CFR 1.132 filed February 16, 2010 is insufficient to overcome the rejection of claims 1, 7-18 and 72 based upon the rejections over the prior art, as set forth in the last Office action because the evidence shows the combination of mouse β-actin promoter and a human CMV enhancer, resulting in significantly higher level of luciferase expression as compared to a construct utilizing a chicken β-actin promoter and a human CMV enhancer, and

not to any species of CMV enhancer, that may include chicken, mouse or rat CMV. Thus, there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716.

The rejection:

The claims embrace a DNA construct wherein a mouse β-actin promoter is operably linked to a CMV enhancer; a vector comprising said construct, and a hamster cell comprising said vector.

Hadjantonakis et al. describe the generation of transgenic mice expressing a GFP marker transgene, wherein the GFP expressing vector drives marker expression by a CMV immediate early enhancer coupled to a the chicken β-actin promoter (Abstract; second columns, p. 80 and 88 limitation of claims 1, 2, 7, 8 and 12). The authors further describe the establishment of ES cell lines by transformation via electroporation, with the vector (first column, p. 80; limitation of claim 22).

While Hadjantonakis et al. do not describe their β-actin promoter as obtained from a mouse, such was known in the prior art.

Estes et al. disclose rodent promoters, including that of hamster and mouse (Abstract), further providing vectors comprising the promoters for expressing heterologous genes of interest in hamster cells such as CHO, HEK and BHK (column 2, lines 9-20; limitation of claims 4, 13 and 17-19). Estes et al. further disclose the nucleotide sequence of the mouse β-actin promoter as SEQ ID NO: 3, and state that the chicken β-actin promoter has been shown to exhibit a higher activity than viral CMV and SV40 promoters, but only when it is linked to a CMV enhancer (column 1, lines 42-45), thus providing the motivation to link a CMV enhancer to other β-actin promoters.

The teachings of Hadjantonakis et al. and Estes et al. are both directed to the expression of genes of interest under the control of β-actin promoters. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine their respective teachings and to substitute the mouse β-actin promoter for the chicken β-actin promoter with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art

would construct such an expression construct in an expression vector as a matter of design choice, which amounts to simple substitution of one known element for another to obtain predictable results. Applicants should note that the *KSR* case forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR International Co. v. Teleflex Inc.*, 550 U.S.-, 82USPQ2d 1385 (2007).

Response to arguments:

Applicants traverse the rejection and argue that the present application discloses a DNA construct comprising a mouse β-actin promoter and a CMV enhancer, that can drive an unexpectedly high level of expression (as in Example 2), showing a significantly higher level of activity than the human EF 1 α promoter (the "CEF promoter"). Applicants' arguments have been fully considered, but are not found persuasive.

In response, it should be noted that the CEF promoter or the mouse β-actin promoter alone, are irrelevant to the subject matter of the instant claims. "[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991). Here, the closest prior art discloses the chicken and mouse β-actin promoters, not the CEF promoter. Further, the prior art discloses a CMV immediate early enhancer coupled to a chicken β-actin promoter.

Regarding Exhibit B of the Declaration under 37 CFR 1.132, it should be again noted that evidence shows the combination of mouse β-actin promoter and a human CMV enhancer, resulting in significantly higher level of luciferase expression as compared to a construct utilizing a chicken β-actin promoter and a human CMV enhancer, whereas the instant claims are not limited to the human CMV enhancer, and encompass any species of CMV enhancer, from any source.

In response to Applicants' argument that the Estes et al. patent discloses a functional promoter, it should be noted that as stated in MPEP 716.07, every patent is presumed valid (35 U.S.C. 282), and that presumption includes the presumption of operability (*Metropolitan Eng. Co. v. Coe*, 78 F.2d 199, 25 USPQ 216 (D.C. Cir. 1935). Affidavits or declarations attacking the operability of a patent cited as a reference must rebut the presumption of operability by a preponderance of the

evidence. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). In the instant case, Applicants have failed to provide any evidence to show that the promoter disclosed by Estes et al., is inoperable. With regard to the single T residue sequence difference, it should be noted that the instant claims have not been limited to any SEQ ID NOS.

Thus, the rejection is maintained for reasons of record and the preceding commentary.

Claims 1, 2 and 5 were previously rejected under 35 U.S.C. §103(a) as being unpatentable over Estes et al. (U.S. Patent No.: 7,423,135; effective filing date Jun. 24, 2003), and further in view of Debs et al. (U.S. Patent No.: 6,468,798; filed Jan. 14, 1998), in the Office action dated August 14, 2009. Applicants' cancellation of claim 2 renders its rejection moot. Applicants' argument that the nucleotide sequence disclosed by Estes et al. differs from the instantly claimed SEQ ID NO: 2 by a single nucleotide is found persuasive. Thus, the rejection is hereby withdrawn.

Claims 1, 7-11 and 14-16 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Estes et al. (U.S. Patent No.: 7,423,135; effective filing date Jun. 24, 2003), in view of Yano et al. (Cytotech. 16:167-178; 1994; of record) and further in view of GenBank BC011083 (2002). The rejection set forth on pp. 6-7 of the previous Office action dated August 14, 2009 is maintained for reasons of record.

The rejection:

The claims embrace a DNA construct wherein a mouse β-actin promoter is operably linked to a CMV enhancer; a vector comprising said construct and a mouse c-Ha-ras oncogene, and a hamster cell comprising said vector.

Estes et al. disclose rodent promoters, including that of hamster and mouse (Abstract), further providing vectors comprising the promoters for expressing heterologous genes of interest. Estes et al. state that the chicken β-actin promoter has been shown to exhibit a higher activity than viral CMV and SV40 promoters, but only when it is linked to a CMV enhancer (column 1, lines 42-45), thus providing the motivation to link a CMV enhancer to other β-actin promoters.

While Estes et al. do not disclose the inclusion of a c-Ha-ras oncogene in their CMV/ β-actin vectors, such was known in the prior art.

Yano et al. describe the c-Ha-ras oncogene as capable of enhancing promoter activity when expressed downstream of the CMV promoter and transactivating β-actin in BHK-21 cells (Title and Abstract), thus providing the motivation to include said oncogene in the vector of Estes et al. The mouse c-Ha-ras gene was known in the prior art as evidenced by GenBank BC011083.

The teachings of Estes et al. and Yano et al. both include the utilization of CMV promoter elements to increase transcription via vector constructs. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine their respective teachings and to include the human or mouse c-Ha-ras oncogene in the vector of Estes et al. with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art would produce such an expression construct in an expression vector to increase promoter activity, and because such was expressly taught by Yano et al.

Response to arguments:

Applicants traverse the rejection and present arguments substantially the same as those previously presented, regarding the teachings of Estes et al. Applicants' arguments have been fully considered, but are not found persuasive. Applicants are referred to the response provided above.

Thus, the rejection is maintained for reasons of record and the foregoing commentary.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Primary Examiner, Art Unit 1633